CLINICAL EXPERIMENT ON LUPUS VULGARIS AND LUPUS MILIARIS DISSEMINATUS FACIEI WITH SINGLE ADMINISTRATION OF CORTICOIDS*

TADAYO MATSUBARA, M.D.

Antituberculous treatment combined with corticoids has been much studied in the field of internal medicine. Recently many reported that this combined therapy was effective against tuberculosis, particularly for meningitis, miliary tuberculosis, exudative pleurisy and pericarditis, and sometimes for active pulmonary tuberculosis.

Longhin (1) and Lapière (2) reported that this combined therapy was effective against cutaneous tuberculosis. Kalkoff (1952) (3) stated that he had treated one case of lupus vulgaris with ACTH for a short period with considerable benefit.

From a practical point of view in the treatment of tuberculosis, corticoids should be used administered simultaneously with antituberculosis remedies. This procedure, however, would make it impossible to determine the effect of the individual remedies.

Therefore, an attempt was made to treat the patients with skin tuberculosis with corticoids only. For this purpose corticoid therapy was administered to patients with lupus vulgaris, a typical cutaneous tuberculosis, and to patients with lupus miliaris disseminatus faciei, one of the tuberculids.

MATERIALS AND METHODS

All of the patients, 7 cases of lupus vulgaris and 9 of lupus miliaris disseminatus faciei, were observed in the skin clinic of Kyoto University. All patients were Japanese. The corticoids used were prednisolone, dexamethasone, triamcinolone or methylprednisolone. An average daily dose of 15 mg. of prednisolone, 1.5 mg. of dexamethasone, 12 mg. of triamcinolone or 12 mg. of methylprednisolone was given until an apparent clinical cure was obtained. The duration of hormone therapy varied in each case.

In lupus vulgaris there was no flare-up of the condition after reduction of the dose or withdrawal of corticoids. Therefore, in lupus vulgaris corticoids were discontinued within a month after clinical cure. But in lupus miliaris disseminatus faciei, there was often a flare-up of the condition after their reduction of the dose or after withdrawal. The dose of corticoids was therefore increased when a flare-up occurred.

In each case of lupus vulgaris two specimens of tissue were obtained by punch biopsy both on admission and during the course of corticoid treatment. One of these was cultured and the other was implanted into the abdominal cavity of a guinea-pig. In 4 of 7 cases tubercle bacilli were demonstrated; these were sensitive to INH.

Chest x-rays taken both on admission and at monthly intervals during corticoids administration. There was no evidence of active pulmonary tuberculosis.

RESULTS

1. *Lupus vulgaris*

Seven patients, 2 males and 5 females, with lupus vulgaris were treated with oral administration of corticoids. The age ranged from 32 to 55 years. Tubercle bacilli were proved in 4 of 7 cases. All patients responded well to corticoids. Skin lesions began to improve within a week, becoming less red and less elevated.

One month later, bacteriological examination was negative for tubercle bacilli in all the cases.

In 2 months, histologic examination revealed that the features of typical tuberculous nodules in skin lesions marked by epithelioid and giant cells were replaced by those of banal inflammation associated with perivascular infiltation of lymphocytes and fibroblasts. There were no active skin lesions in any case after 4 to 8 months' corticoids administration. When clinical symptoms subsided corticoid therapy was discontinued. The histories of 3 representative cases are as follows.

Case 1. A 34-year-old female with a past history of Pott's disease at the age of 24, and lupus vulgaris at 31 which worsened gradually leaving characteristic plaques of small tubercles on the face. She had never been put on antituberculosis remedies. Both chest x-rays for tuberculosis and culture and animal experiment for tubercle bacilli were negative on admission. Following administration of dexamethasone in daily doses of 1.5 mg., the skin lesions began to improve within a week, becoming less red and less elevated.

A bacteriologic examination for tubercle bacilli

* From the Department of Dermatology, Kyoto University, School of Medicine, Kyoto, Japan.

Received for publication April 5, 1961.

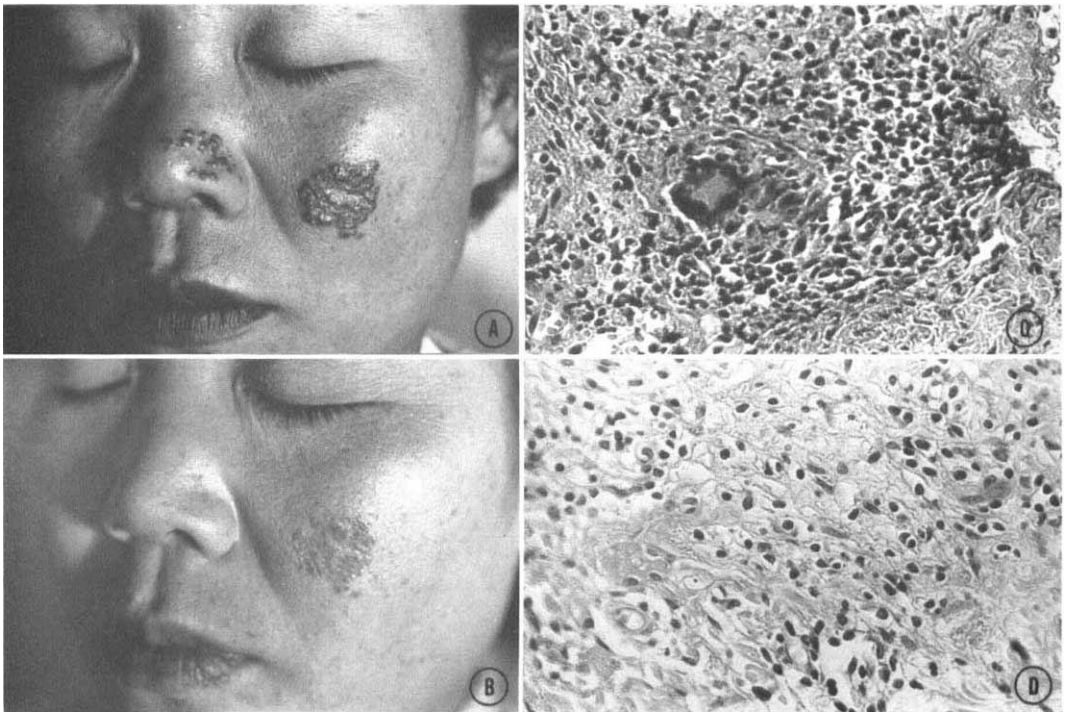

FIG. 1

carried out one month later was also negative. The papular lesions were flattened in 77 days with histologic features of banal inflammation replacing typical tuberculous nodules found on admission (Fig. 1 (a)–(d)).

Dexamethasone was discontinued and methylprednisolone administered in daily doses of 12 mg. in about 9 weeks when secondary corticoid effects developed (acne, marked moon face and increase of appetite and weight). Thereafter the appetite and weight returned almost to normal, though the acne and moon face persisted.

The corticoid was given in gradually decreasing doses after clinical cure was established in 133 days, and was discontinued in a month thereafter.

Case 2. A 55-year-old female with long-lasting, progressive, centrifugal plaque of small tubercles on the right side of the neck since the age of 24. Chest x-rays for tuberculosis and culture and animal inoculation for tubercle bacilli were negative. Prednisolone 15 mg. daily was given. Some improvement of the lesion was observed within one week. After a month bacteriological examination of the lesion for tubercle bacilli was again negative. Two months' treatment resulted in the flattening of tubercles in the lesion and in a change of histologic features from typical tuberculous nodules to that of a banal inflammation.

The tubercles disappeared in 4 months leaving flattened scars (Fig. 2 (a)–(b)). There was no side-effect except for a slight degree of moon face. Prednisolone was gradually reduced and finally discontinued one month after the clinical cure.

Case 3. A 32-year-old male with a history of lupus vulgaris since 16 years of age. The lesions spread from the lateral angle of the left orbit to both sides of the cheeks and ears, the nose, the upper lip and the left side of the neck, leaving irregular scars with nodules and ulcers around them in the corresponding regions. A skiagram revealed no underlying bone changes. The patient had never been given antituberculosis remedies. Both the culture from the lesions and animal inoculation were positive for mycobacterium tuberculosis. Chest x-rays were negative on admission. Prednisolone was given 15 mg. daily and was followed by some improvement of the lesions within a week.

After 34 days, both culture and animal inoculation were negative for *Mycobacterium tuberculosis.*

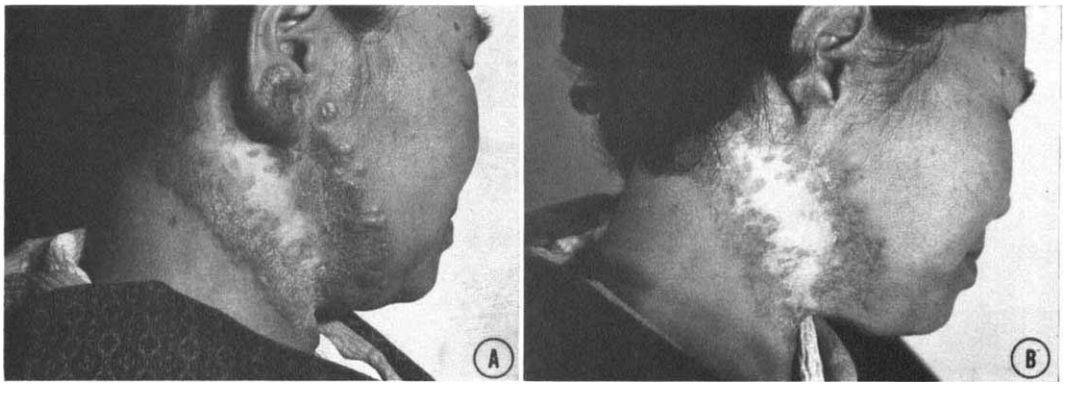

FIG. 2

After 9 months' treatment, the histology were marked by perfect epithelization of ulcers and banal inflammation replacing typical tuberculous nodules.

The dosage was gradually reduced after the clinical cure was obtained in 4 months and all medications were discontinued 5 months after the start treatment. A slight relapse of the ulcers appeared 10 months after discontinuance of the treatment. Prednisolone was again prescribed (15 mg. daily), and the clinical symptoms subsided in a month.

In 4 cases of the 7, INH was administered to ensure the permanent cure after the dramatic improvement with the single course of corticoid. The INH medication was continued for about 2 years with successful control of the disease. However, 2 of the 3 cases treated without supplementary INH therapy, slight recurrences of the lesions occurred in 2 patients after about one year of the discontinuance of corticoids and necessitated resuming corticoid therapy. One corticoid-treated case without supplementary INH has remained cured for 2 years after the discontinuance of corticoids.

2. Lupus miliaris disseminatus faciei

Nine patients, 5 males and 4 females, with lupus miliaris disseminatus faciei were treated with corticoid. The age ranged from 21 to 46 years. All patients had non-ulcerative tubercles with the exception of 2 patients who did have ulceration.

All patients received desamethasone in daily doses of 1.5 mg. Some of the maculopapular lesions disappeared within 2 weeks. Most of papular lesions were flattened after 1 to 2 months' treatment. (Fig. 3 (a)-(b)). After 4 to 6 months' treatment all the lesions were flattened with cicatricial healing. Dexamethasone was then gradually reduced. As relapses occurred in all the cases, the original dosages were resumed. Thereafter the maintenance dose necessary for clinical cure for each patient was determined. In 5 of the 9 patients, the maintenance doses were given in combination with INH. The combined therapy was continued for 1 to 2 years and complete cure was obtained in these 5 cases within 3 years.

The remaining 4 cases (including the above-mentioned exceptional 2 cases with necrotic ulcers) were treated only with corticoids and were cured within 3 years. All of the 9 patients have had no recurrences for over 6 months.

In each case histologic examination was done on admission, after a month's treatment and when apparent clinical cure was obtained after 4 to 6 months' treatment. In the lesions treated for a month, fewer epithelioid cells, fewer giant cells and many more fibroblasts were found (Fig. 3 (c)-(d)). In the lesions showing apparent clinical cure, the histologic features were found to have changed from typical tubercles to banal inflammation with extensive fibrosis.

COMMENTS

Corticoid therapy for lupus vulgaris and lupus miliaris disseminatus faciei was studied. In this experiment, antituberculosis remedies ordinarily given in combination with corticoids, were not administered during certain periods in order to observe the effect induced only by the latter.

In each case, chest x-rays were negative for tuberculosis at the first consultation. Extreme

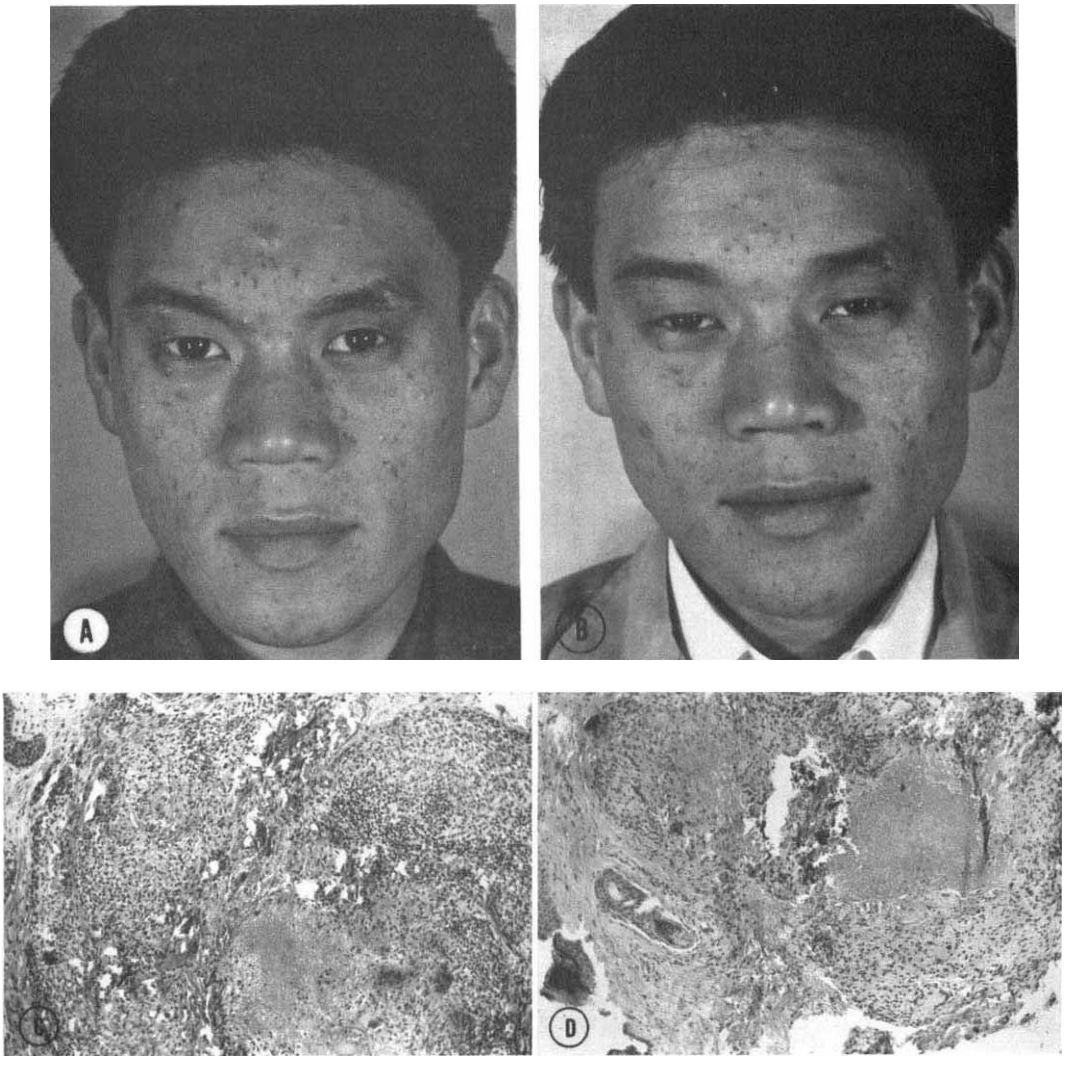

FIG. 3

care was taken to observe possible side-effects of the drug; and chest x-rays repeatedly taken during the course of corticoid administration were all negative for pulmonary tuberculosis.

In all the cases of lupus vulgaris the clinical symptoms were successfully controlled by the administration of corticoids. Both culture and animal inoculation of the lesions were negative for tubercle bacilli after a month of treatment. After the clinical symptoms subsided, corticoid therapy was discontinued. Thereafter 3 of 7 cases were observed and found not to require further medication. Slight recurrences of the lesions occurred in 2 of these 3 cases about one year after discontinuance of the treatment. The other 4 cases out of 7 were treated with INH after discontinuance of corticoids. No relapses occurred for 2 years in all the cases treated with INH (and one case with no antituberculosis remedies) after discontinuance of corticoids. As relapses occurred in about one year only in those cases to which no antituberculosis remedies were given following the successful management by corticoids, it seems reasonable to assume that the bacilli remained, more or less, in the lesions even when clinical cure was established.

In all cases of lupus miliaris disseminatus faciei treated with corticoids, clinical symptoms sub-

sided and histologic features of tuberculous nodules were replaced by those of banal inflammation with fibrosis. Then, reduced doses of corticoids were given in 5 of 9 cases in combination with antituberculosis remedies and in the remaining 4 cases with no antituberculosis remedies. Although relapses of varying degree occurred in all the cases, all of the patients were finally cured.

There were no apparent differences between the clinical course of the 4 cases treated without additional antituberculosis remedies and that of the 5 cases having the combined therapy.

Corticoids are especially useful for cosmetic purpose both in lupus vulgaris and in lupus miliaris disseminatus faciei, since the former most frequently and the latter with no exception occur on the face, leaving scars.

However, for practical considerations, it is recommended that the antituberculosis remedies be combined with the corticoids.

SUMMARY

A clinical trial of corticoid therapy in lupus vulgaris and lupus miliaris disseminatus faciei is reported.

The results of therapy were excellent without supplementary use of antituberculosis remedies.

REFERENCES

1. S. Longhin, Teodosiu, T. Dumitrescu, A. and Rosu, P.: Die Corticoidbehandlung der Hauttuberculose. Dermato.-vener. (Bucuresti), **3:** 59–63, 1958.
2. S. Lapiere: Les corticostéroïdes pour le traitment de cas rebelles de tuberculides papulonécrotiques et noduliares. Dermatologica (Basel), **117:** 354–361, 1958.
3. K. W. Kalkoff: Zur Rückbildung des Lupus vulgaris nach ACTH. Klin. Wschr., **30:** 330–333, 1952.